

10531847

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CENTRAL FAX CENTER  
JUN 13 2008

yes  
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In the Specification

At Page 1, paragraph 2, insert the following:

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**FEDERALLY-SPONSORED RESEARCH OR DEVELOPMENT**

This invention was made with Government support under contract 9910949 awarded by the National Science Foundation. The Government has certain rights in this invention.

AMENDMENTS TO THE SPECIFICATION:

<sup>0055</sup>  
Please replace paragraph [0057] with the following rewritten paragraph:

<sup>0055</sup>  
[0057] For the purposes of the present invention, toxic gliadin oligopeptides are peptides derived during normal digestion of gliadins and related storage proteins as described above, from dietary cereals, e.g. wheat, rye, barley, and the like, by a Celiac Sprue individual. Such oligopeptides are believed to act as antigens for T cells in Celiac Sprue individuals. For binding to Class II MHC proteins, immunogenic peptides are usually from about 6 to 20 amino acids in length, more usually from about 10 to 18 amino acids, and as demonstrated herein, a particularly stimulatory toxic gliadin oligopeptide is the multivalent 33-mer described above. Such peptides include PXP motifs, for example the motif PQPQLP (SEQ ID NO:8). Determination of whether an oligopeptide is immunogenic for a particular patient is ~~readily~~ readily determined by standard T cell activation assays known to those of skill in the art. Illustrative toxic gliadin oligopeptides of the invention are described in Examples 1 and 2 below. The 33-mer gliadin oligopeptide of Example 2 and its deamidated counterpart formed by tTGase are preferred toxic gliadin oligopeptides of the invention.

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<sup>0086</sup>  
Please replace paragraph [0088] with the following rewritten paragraph:

<sup>0086</sup>  
[0088] Tissue transglutaminase (tTGase), an enzyme found on the extracellular surface in many organs including the intestine, catalyzes the formation of isopeptide bonds between glutamine and lysine residues of different polypeptides, leading to protein-protein crosslinks in the extracellular matrix. The tTGase enzyme is the primary focus of the autoantibody response in Celiac Sprue. Gliadins, secalins and hordeins contain several sequences rich in Pro-Gln residues that are high-affinity substrates for tTGase; tTGase catalyzed deamidation of at least some of these sequences, such as, in particular, the 33-mer oligopeptide of the invention, dramatically increases their affinity for HLA-DQ2, the class II MHC allele present in >90% Celiac Sprue patients; and presentation of these ~~deamidate~~ deamidated epitopes by DQ2 positive antigen presenting cells effectively stimulates proliferation of gliadin-specific T cells from intestinal biopsies of most Celiac Sprue patients. Proposed toxic effects of gluten include immunogenicity of the gluten oligopeptides, leading to inflammation, including by a mechanism in which gliadin peptides directly bind to surface receptors.

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